CHAPTER IX: LINEAR POLYSACCHARIDES

Let's change gears for a minute and look at the linear polysaccharides. And, I'm going to use this glycosaminoglycan family, chondroiton, heparin, heparin sulfate, as an example to illustrate some of the key features.

Here's a cartoon of the cell. And, one of the interesting aspects of these molecules are the fact that they're virtually found on all cells, every mammalial cell, have these polysaccharide coat on them, and they're also at the cell surface, extra cellular matrix interface, and act as a reservoir for storing a variety of molecules, growth factors, cytokines, kimakinds, enzymes. In many ways, they play a role in how a cell process these various signals outside the cell, so that they can dramatically start affecting the cellular functions, in terms of the various signal transaction pathways.

If you actually zoom in, here are these antlike structures that I showed you earlier on, with the protein chain structure with the polysaccharide chains that radiate out.

In many ways, these polysaccharide chains act as a platform where a variety of signaling molecules bind to them in sequence specific fashion, and these molecules, they're not presented to a cognate receptor on the cell surface.

So, it is very important to begin to understand, if you're looking at a variety of signaling molecules, such as, you know, fibroblast growth factor, or transforming growth factor, or IL8, interleukin 8, etc., just to name a few. How they come from the outside, bind to these molecules, get presented to a cognate receptor to activate various signaling events.

Now, when you zoom in, in terms of the structural details, this is where it gets both fascinating but complex. There are many different building blocks that get assembled. Unlike having four bases that make DNA, twenty amino acids to make proteins, with glycosaminoglycans and heparin and heparin sulfate, as an example, there are at least forty-eight possible modification, and you can begin to see the chemical diversity associated with these molecules. And, there are analogous to how DNA binds to proteins, minimal binding sequences that present different factors to these kinds of molecules so that they can modulate signals.

And, what's also fascinating if you actually zoom in further from the point of view of unique structural attributes of these sugar sequences, they behave very similar to DNA, that there are structural modifications in the backbone, such as over winding or under winding of the helix to lead to a formation of a kink that you see in DNA to make optimal contact with proteins to either turn on a signaling pathway or, in many instances, even turn off.

So, we're just beginning to understand and the molecular aspects of these interactions, and, obviously, the question is, then, how does the molecular aspect eventually translate to some of the biological and physiological properties.